REMARKS

Claims 2, 3, 8, 10, 11, 12-13 and 18-21 are pending in the present application and under examination. In the Office Action mailed on March 2, 2006, claims 2-3 were allowed. Claims 8, 11-13 and 18-21 were rejected. Claims 1, 4-7, 9 and 14-17 are canceled. Claims 8, 11-13, and 19-21 have been amended.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the cancelled or unamended claims.

Since the specification provides support for each of the above amendments, entry of these amendments is respectfully requested. The amendments do not introduce new matter. Support for the recitation "immunogenic" may be found throughout the application and is already included in pending claim 18.

I. REJECTIONS UNDER 35 U.S.C. 112, Second Paragraph

Claims 8, 11, 12, 13, and 19-21

Claims 8, 11, 12, 13 and 19-21 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for reciting nucleic acids with percent identity to a given sequence but without a stated function.

Applicants respectfully traverse the Examiner's rejection and its supporting remarks. A claim to a composition does not need to include the use of the composition. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer, to include the recitation "immunogenic."

Thus, Applicants respectfully request that the Examiner withdraw the rejection of claims 8, 11, 12, 13 and 19-21 under 35 U.S.C. § 112, second paragraph.

Claim 11

Claim 11 has been rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite.

Applicants respectfully traverse the Examiner's rejection and its supporting remarks. However, in order to facilitate prosecution in this case applicants have amended the pending claim, without prejudice or disclaimer, to include the recitation "fully."

Thus, Applicants respectfully request that the Examiner withdraw the further rejection of claim 11 under 35 U.S.C. § 112, second paragraph.

II. REJECTIONS UNDER 35 USC 112, First Paragraph, Enablement

Claims 8, 12, 13 and 18-21 have been rejected under 35 USC 112, first paragraph, for allegedly failing to enable isolated nucleic acid sequences which have 50% or greater identity to an isolated nucleic acid sequence set forth in SEQ ID NO:3, isolated nucleic acid sequences which encode 10-mer fragments, and isolated nucleic acid sequences which are 80-95% identical to SEQ ID NO:3 with no stated function.

Specifically, the Examiner has asserted that the claims are not enabled due to alleged lack of specific guidance, the unpredictability regarding which amino acids can be changed while still maintaining the function of the nucleic acids of the invention, and the expense and time-consuming nature of the experimentation required to practice the invention.

Applicants respectfully traverse the Examiner's rejection and its supporting remarks.

A. No *prima facie* case

The specification must be taken as complying with the first paragraph of § 112 unless there is a reason to doubt the objective truth of the statements relied upon therein for enabling support (*In re Marzocchi*, 169 USPQ 367 (CCPA 1971)). The Examiner has not provided any reason to doubt

that the specification is enabling for making or using of the presently claimed invention. As support for her enablement rejection, the Examiner cites to two articles. However, neither of these articles supports a *prima facie* case for lack of enablement of the presently pending claims for the representative use of the claimed nucleic acids for expression of immunogenic polypeptides, as both articles cited by the Examiner relate only to the structural requirements for maintaining biological function, e.g., catalysis of proteins, not to the requirements for an encoded polypeptide having immunogenicity. Section 2164.01(c) of the MPEP states that:

> When a compound or composition is limited by a particular use, enablement of the claim should be evaluated based upon that limitation.
>
> In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection based upon how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple use are disclosed, the application is enabling for the claimed invention. (citation omitted)

The specification on page 45, line 18 through page 46, line 6 discusses use of *Neisserial* antigens in immunodiagnostic assays for detecting antibody levels and such *Neisserial* antigens may be expressed using nucleotide sequences as claimed as discussed in the specification beginning on page 8, line 16. Thus, one use of the immunogenic polypeptides is to detect antibodies to *Neisserial* antigens in the blood of a patient to determine whether the patient has been infected with a *Neisserial* pathogen. In order to establish a *prima facie* case of lack of enablement, the Examiner must provide evidence that the representative use of expression of a immunogenic polypeptide is not enabled.

B. Unpredictability

The Examiner appears to believe that a claim is only enabled if one is able to predict the exact sequence of every nucleic acid with the particular use within the claim scope. However, by

analogy to the monoclonal antibodies in *In re Wands*, this is not an absolute requirement for enablement, 858 F.2d 731 (Fed. Cir. 1988). Under *Wands*, it is well established that claims to monoclonal antibodies directed to a particular protein are enabled even where the application only discloses the sequence of the protein. Clearly, with just the protein sequence, one of skill in the art could not predict the sequences of even a single monoclonal antibody, much less all monoclonal antibodies that could bind to the protein. Nevertheless, in *Wands*, the Federal Circuit still found such claims to be enabled on the grounds that is routine for one of skill in the art to immunize an animal such as a rabbit with the protein, generate monoclonal hybridoma from the rabbit and screen them for monoclonal antibodies which are directed to the protein.

The representative use of the presently claimed nucleic acids is analogous to the monoclonal antibodies' function as claimed in *Wands*. In *Wands*, the biological molecules were monoclonal antibodies with the function of binding to HBsAg. With the present claims, the biological molecules are nucleic acids which may be used for expression of an immunogenic polypeptide. Furthermore, as in *Wands*, one of skill can practice the presently claimed invention using routine procedures known to those of skill in the art. To identify sequences that encode immunogenic polypeptides, one of skill need only use a routine procedure of synthesizing nucleotide sequences, expressing the encoded protein using standard expression vectors, and screening polyclonal antibodies obtained from blood of an animal that was immunized with a *Neisserial* bacteria for antibodies that recognize the encoded polypeptide. Screening polyclonal antibodies is a simpler task and even more routine than generating hybridomas and screening monoclonal antibodies produced from them as was found routine and therefore enabled under *Wands*. Thus, under the standard expressed in *Wands*, the present claims are enabled even though the application may not disclose the sequence of every nucleic acid in the present claim scope which will function for the representative use.

Thus, the present claims are enabled because there are well-established, routine methods of screening that will predictably identify nucleic acids for use in expressing immunogenic polypeptides and therefore no undue experimentation is required to determine conditions for use of a nucleic acid within the scope of the claims.

C. Amount of Guidance Required

The Examiner has also asserted that the present application lacks sufficient specific guidance regarding which amino acids can be changed while still maintaining the function of the nucleic acids of the invention. As discussed above, this is not relevant to the representative use presently discussed because the use does not require that the protein be functional. The representative use merely requires that some fragment thereof remain immunogenic. Further, working examples are not required to enable an invention. See, *e.g.*, MPEP §2164.02; In re Borkowski, 422 F.2d 904, 908 (CCPA 1970). It is well established that guidance need not be provided for the methods if they are readily available to one of skill in the art. See, *e.g.*, MPEP §2164.01 ("A patent need not teach, and preferably omits, what is well known in the art."). The skill in the art with respect to the presently claimed invention is quite high. These nucleic acids are typically generated by research scientists who are at least Ph.D. level with a fair amount of post-doctoral experience or relevant industry experience. Thus, those of skill in the art are highly capable individuals with a high degree of familiarity with the screening methods needed to identify nucleic acids as claimed.

Further, the application provides ample specific guidance regarding the location of immunogenic epitopes for use in expressing immunogenic polypeptides. On page 48, lines 23 to 28, the specification identifies and provides citations to references describing three well-established methods for identifying antigenic fragments: hydrophilicity plot, antigenic index, and AMPHI analysis. Using these methods, it is routine for one of skill in the art to identify regions that are immunogenic and to avoid making changes in these regions when synthesizing nucleic acids for screening. Applicants further have provided their own hydrophilicity, antigenic index, and AMPHI analysis of SEQ ID NO: 4 in Figure 4E of the specification. Therefore, instead having to randomly determine which nucleic acid substitutions will maintain immunogenicity of the encoded polypeptide, one of skill in the art merely has to look at the provided data and use this as a guide for synthesis of nucleic acids.

D. Quantity of Experimentation

Contrary to the Examiner's assertions, the expense and time required to identify sequences within the claim scope are irrelevant to the question of whether the experimentation is undue. The expense of experimentation is not one of the Wands factors listed in MPEP §2164.01. Further, MPEP § 2164.06 explicitly states that neither the time nor difficulty of experiments are determinative if they are merely routine. As described in the above section, the screening methods required to practice the claimed invention are routine to those of skill in the art (or at the very least more routine than the screening methods in *Wands* in which the claims were enabled).

As made clear in *In re Wands*, a considerable amount of experimentation is permissible if it is merely routine. 858, F.2d 731 (Fed. Cir. 1988). In *Wands*, the Federal Circuit held that "in the monoclonal antibody art it appears that an 'experiment' is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen. This process entails immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics." 858, F.2d at 740. The Federal Circuit further noted that, "[p]ractitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody." 858, F.2d at 740. The "experiment" of identifying nucleic acids that may be used for either representative use involves design and synthesis of a family of nucleic acids of a particular sequence and then screening for applicability to the use. Therefore, by analogy to monoclonal antibodies, it does not matter that one of skill in the art may have to spend considerable time and expense screening more than one nucleic acid to find one with applicability to the representative use.

E. Summary

Thus, Applicants respectfully request that the Examiner withdraw the rejection of Claims 8, 12, 13, and 18-21 based upon 35 U.S.C. § 112, first paragraph, enablement. Just as in *Wands*, the presently claimed invention may be practiced by routine screening methods that will allow one of skill in the art to use claimed nucleic acids commensurate in scope for the representative use discussed above. The guidance in the specification is sufficient given the routine nature of the screening methods to those of skill in the art. The mere fact that the screening methods may be time-consuming and expensive fails to support the Examiner's rejection.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002099101. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

By _____

Otis Littlefield
Registration No.: 48,751
MORRISON & FOERSTER LLP
425 Market Street
San Francisco, California 94105-2482
(415) 268-6846